Clinical Data Update System (CDUS)
Frequently Asked Questions

CDUS Version 3.0

March 12, 2003

The questions listed below are some of the more commonly asked questions that CTEP has received related to the Clinical Data Update System (CDUS), version 3.0. Please refer to the following publications if further information is needed. All publications are available in PDF format from CTEP's CDUS Web page at http://ctep.cancer.gov/reporting/cdus.html.

Specifically written for FTP submitters, DBAs, and database engineers:

- **Clinical Data Update System (CDUS) Instructions and Guidelines**
- **CDUS - Notice of Modifications v3.0**

Specifically written for CDUS Web Application users:

- **CDUS v3.0 Web Application Online Help (available within the** application**)**
- **CDUS v3.0 Web Application Quick Reference Guide**

If, after referring to this document and/or the above publications, you are unsuccessful in obtaining answers to your questions, please contact the NCI CTEP Help Desk at (301) 840-8202, or by e-mail at **ncictephelp@ctep.nci.nih.gov**.

1. What version of CDUS should I use?

As of July 1, 2002, all CDUS submitters are required to follow the information provided in the *CDUS Instructions and Guidelines*, version 3.0, which is posted on the CTEP Home page located at http://ctep.cancer.gov/reporting/cdus.html.

2. How may I submit my data to CDUS?

Data may be submitted electronically using one of the following two mechanisms (paper or hard copy submissions are not acceptable):

FTP (File Transfer Protocol) – FTP is the preferred method where data are electronically sent to CTEP's FTP site at ftpctep.nci.nih.gov. This method requires Internet access and the development of computer programs to download your data from your database to the CDUS. This method should alleviate the need for duplicate data entry. The file format used is described in the *CDUS - Smart Loader File Format Instructions* section (section 4) of the *CDUS Instructions and Guidelines*.

CDUS Web Application – Data submission can also be performed using the Web-based data entry application. This application, recently improved as of July 1, 2002, provides a user-friendlier environment with pull down menus, field and screen instructions; pre-populated fields; and a report to validate your data prior to submission. Please be advised that Internet Explorer 5.0 or higher is recommended to access the CDUS Web-based application and that the application has *never been tested to support a MAC/Apple computer*.

Both mechanisms require establishing user accounts; please e-mail the NCI CTEP Help Desk at ncictephelp@ctep.nci.nih.gov to request a user account.

3. I have an MAC/Apple and will be submitting CDUS data using the Web-based data entry system. Will I have difficulty submitting?

The CDUS Web-based application has never been tested to support a MAC/Apple computer. For optimum performance, it is recommended that a personal computer with Internet Explorer 5.0 or higher be used to access the secured Web application. Commercially available virtual PC software (e.g., Connectix Virtual PC™ for Mac®) may help MAC/Apple users to run the CDUS application, however, CTEP cannot guarantee their success.

4. What new data elements are required with CDUS v3.0 and how do I know if I am required to submit this data for my protocol?

As of July 1, 2002, CTEP is collecting the following additional data (compared to CDUS v2.0) for all studies regardless of activation date:

- A patient's ethnicity,
- A patient's race or races (as patients may now have multiple races documented), and
- The date that the current trial status was assigned.

In addition to the above, the following are required for studies activated on or after January 1, 2002:

- The number of samples collected and the number of samples analyzed (applies to correlative study protocols or protocols with embedded correlative studies).

In addition to the above, the following is required for studies submitted via CDUS-Complete:

- The date of the patient's last treatment,
- The reason the patient went off study and the date it occurred,
- The indication that abnormalities were found during a patient's baseline examination (e.g., initial history, physical examination), and
- Late Adverse Events.

Several of the data elements are required for all protocols (e.g., Current_Trial_Status_Date); while other data are dependent on the activation date of the trial (i.e., Baseline_Abnormality will be mandatory data for studies activated on or after 01/01/2002, please see questions 11 and 12 for additional information) or dependent of the existence of other data within the collection (e.g., correlative studies).

Please refer to the *CDUS Notice of Modifications* for more information on the requirements. This document can be found on the CTEP Home Page at http://ctep.cancer.gov/reporting/cdus.html.

5. Can we submit the new data for protocols activated before 01/01/2002 as well as for protocols activated on or after 01/01/2002?

Yes, the new data may be submitted for any study; however, these data are mandatory only for studies activated on or after 01/01/2002. The CDUS v3.0 includes business rules that validate the inclusion of new data for studies meeting the activation date criteria (refer to the *CDUS Business Rules* section (section 9) of the *CDUS Instructions and Guidelines* for more information). However, the CDUS does not validate this data for studies activated prior to 01/01/2002 and therefore relies on other business rules to ensure accurate data submission. Please be advised that by submitting this data, you may be required to include other mandatory data. For example, if you submit an Off_Study_Reason, then you must submit an Off_Study_Date or your submission will reject.

6. Will CDUS accept a partial data submission?

This depends on the data being submitted. If the missing data is an incomplete, incorrect, or inappropriate mandatory data element or an incorrect requested data element, the entire data set will be rejected. The re-submitted data set must resolve all identified errors before the file will load successfully. Please refer to the *Definitions for Mandatory, Requested, and Optional* section (section 7.2) and the *Definitions for Incomplete, Incorrect, Inappropriate, and Inconsistent* section (section 7.3) of the *CDUS Instructions and Guidelines* for more information.

7. Recently, CDUS requested that we provide the current status and date with our CDUS submission. What are these and where do we find these?

The Current Trial Status is the status presently assigned to the study by the Lead Organization using CTEP definitions. For the descriptions of CTEP's definitions of statuses and the appropriate codes, please refer to the *Current Trial Status* section (section 2.1.1.5) of the *CDUS Instructions and Guidelines*. The Current Trial Status Date is the day that the Current Trial Status was assigned to the study.

Note: The Current Trial Status and Current Trial Status Date are displayed as part of the Expected List sent to all designated CDUS contacts at the beginning of the quarter. If, during the course of processing your submission, the status and status date are updated, then you must also update that data in your submission.

8. Does the Current Trial Status of 'Closed to Accrual and Treatment (CB)' apply to a non-treatment protocol?

No, the status of 'CB' does not apply to non-treatment protocols. Non-treatment protocols should typically progress through the Current Trial Status codes of 'Approved (AP),' 'Active (AC),' 'Closed to Accrual (CL),' 'Complete (CP).'

9. My study has been approved by CTEP but we have not yet started accruing patients. When do I start to submit data and for how long must I continue to submit data?

Submitting CDUS data to CTEP is required the quarter after the approval of your study regardless of patient accrual. If no patients are accrued, then only the Collections information is submitted. For example, if your study was approved in the months of September, October or November, you would be required to submit by January 31. Please refer to the *Summary of CDUS Reporting Requirements for Cooperative Groups and CCOP Research Based trials* table (Table A) and the *Summary of Reporting Requirements for Non-Cooperative Group (Cancer Centers and other Institutions) Trails Utilizing DCTD Agents of Grant Funding (if CDUS reporting is a grant requirement)* table (Table B) of the *CDUS Instructions and Guidelines* for all due date and approval range information. Refer to the *COLLECTIONS Table* section (section 4.3.1) to identify the data required for the Collections information submission.

You are required to submit cumulative data each quarter, throughout the life of the study, until this study has a Current Trial Status of Complete (CP) or Administratively Complete (AD). Please refer *Current Trial Status* section (section 2.1.1.5) of the *CDUS Instructions and Guidelines* for Current Trial Status definitions.

10. Please clarify the difference between IMT and MedDRA codes. Which should I use?

As of July 1, 2002, CDUS submitters are required to use the Medical Dictionary for Medical Affairs (MedDRA) codes, version 5.0 for Disease, Therapy, Adverse Event, and Pre-Existing Condition information. These codes are posted on the CTEP Home page under the *List of Codes and Values* heading located at http://ctep.cancer.gov/guidelines/values.html. The MedDRA v5.0 codes replace the previously used MedDRA v1.99 codes, which were also referred to as the International Medical Terminology (IMT) codes. A mapping of the IMT codes to the MedDRA v5.0 codes is also available from the above address (see the Mapping Version Excel [.xls file]).

11. What is a Baseline Abnormality?

Baseline Abnormality is defined by CTEP as any abnormal assessment (e.g., physical finding, subjective complaint, or diagnostic test abnormality) identified as part of the

routine pre-study work-up for which an Adverse Event term exists in the Common Toxicity Criteria (CTC) document.

12. Please clarify the new reporting requirements for Baseline Abnormalities. We know that some data are required for all patients on studies activated on or after 01/01/2002. What about those patients accrued to a study after 01/01/2002 but the study was activated before 01/01/2002, must these patients be included in this new requirement also?

No, the reporting requirement is based on the protocol's activation date not on the patient's Date of Entry. Hence, a patient's Date of Entry date has no bearing on the requirement. CTEP requires the new reporting data if the study was activated on or after 01/01/2002 and is CDUS-Complete monitored. CTEP does not expect Baseline Abnormality data for any patient accrued to a study activated before 01/01/2002 regardless of the patient entry date. Please be advised that although it is acceptable to provide this additional data, you may be required to include other mandatory data or your submission will reject. For example, if the Baseline Abnormalities Flag is 'Yes,' then other Baseline Abnormalities information must be provided.

13. There is reference in the *CDUS Notice of Modifications* about confusion regarding Eligibility vs. Ineligibility status. Please explain further.

The Eligibility_Status data element in the CDUS v2.0 was renamed Ineligibility_Status to avoid misinterpretation. CTEP asks that all submitters review how they interpret this question, the question being "Has the patient been declared *ineligible*?" and remember that a patient is considered eligible until declared ineligible.

14. If a patient is determined ineligible before the patient's data are entered in CDUS, do I still have to report that patient?

If the patient is registered, then the patient's data are required and reported as ineligible. Please refer to the *Ineligibility Status* section (section 2.2.2.7) of the *CDUS Instructions and Guidelines* for more information.

15. Please explain the correct use of the Registering Group ID of 'CTSU' for CDUS reporting purposes and where would I go to find more information about this?

For CDUS reporting purposes, follow the instruction below based on the patient registration conditions.

a. Use the value 'CTSU' only under the following conditions:
   The patient was registered through the CTSU Data Operations Center
   AND
   The patient is not accrued from a cooperative group institution or investigator.

b. Use the appropriate Cooperative Group ID as the Registering Group ID if:

The patient was or was not registered through the CTSU Data Operations Center
AND
The patient was accrued from a Cooperative Group institution or investigator.

c. Use the value of 'Other' if:

The patient was NOT registered through the CTSU Data Operations Center
AND
The patient was NOT accrued from a Cooperative Group institution or investigator

For additional information, visit the Clinical Trials Support Unit (CTSU) Web page located at www.ctsu.org.

16. I am confused about what is and what is not required when reporting Adverse Events to the CDUS. Will my file be rejected if I submit data that is against the recommended guidelines?

Please refer to the *Routine Adverse Event Reporting Guidelines for CDUS* table (Table E) (included below) of the *CDUS Instructions and Guidelines*. The requirements were revised from CDUS v2.0 to v3.0. It is now required to report Grade 3 Adverse Events with an attribution of Unrelated or Unlikely via the CDUS. Reporting Grade 1 or Grade 2 Adverse Events with attributions of Unrelated or Unlikely will not cause a file to be rejected unless there is another reason for the rejection.

Routine Adverse Event Reporting Guidelines for CDUS

Attribution	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Unrelated			CDUS	CDUS	CDUS
Unlikely			CDUS	CDUS	CDUS
Possible	CDUS	CDUS	CDUS	CDUS	CDUS
Probable	CDUS	CDUS	CDUS	CDUS	CDUS
Definite	CDUS	CDUS	CDUS	CDUS	CDUS

17. For coding purposes, I intend to submit a Grade 1 or 2 Adverse Event with an attribution of Unrelated or Unlikely. How do I submit this and not be rejected?

If you choose to report a Grade 1 or Grade 2 Adverse Event with an attribution of Unrelated or Unlikely, you must answer 'Yes' to the question “Has the patient experienced an Adverse Event?” If you choose not to report the Grade 1 or Grade 2 Adverse Event with an attribution of Unrelated or Unlikely, then answer 'No.'

18. Many of my errors are an R0014 for an invalid value of an Adverse Event grade. Where can I go to locate appropriate valid values for an Adverse Event?

Please refer to the Common Toxicity Criteria (CTC) document, v2.0 (Publish Date April 30,1999), or the CTC Interactive Application located on the CTEP Home Page at: http://ctep.cancer.gov/reporting/ctc.html. Both provide valid values for Adverse Events and definitions of each grade. The CTC Interactive Application includes three different search engines to locate Adverse Events and provides a data entry feature from which reports can be generated.

Note: The CTC includes grades zero (0) through five (5) for each Adverse Event. Grade 0 is considered normal, grades 1 through 4 include the definitions from which the Adverse Event can be graded, and grade 5, when appropriate, is a fatal Adverse Event. The CTC document, v2.0, only lists grades 0 through 4 (it is understood that Grade 5 for any Adverse Event is death).

Additional information and general definitions of the grading scale can also be found in the *Patients Experiencing an Adverse Event* section (section 2.2.3.9.2) of the *CDUS Instructions and Guidelines*.

19. What criteria does CTEP prefer in determining the appropriate attribution for an Adverse Event?

All attributions, reported via CDUS, are to be determined by evaluating the relationship between the documented Adverse Event and the investigational agent(s) being used on the trial. Please refer to the *Attribution* section (section 2.2.3.9.2.4) of the *CDUS Instructions and Guidelines* for specific attribution code, description, and definition information.

20. I am requesting more information on Late_Adverse_Events. Which grades and attributions are reported and when is an Adverse Event considered late?

Late_Adverse_Events are reported regardless of whether they have been identified as part of a scheduled or an unscheduled follow-up.

All Adverse Events reported to the CDUS will be associated with a specific treatment course. However, events that occur after the treatment is complete and/or when the patient is no longer considered within the time frame to record the event as part of the last treatment course is considered a Late Adverse Event as it cannot be associated with a specific Course_ID or course of treatment.

The same grades and attributions are used to report Late_Adverse_Events as are used to report an Adverse_Event. Please refer to the *Common Toxicity Criteria* (CTC) located on the CTEP Home page at http://ctep.cancer.gov/reporting/ctc.html.

21. How should I report a Late Adverse Event for studies activated before 01/01/2002?

Before the implementation of CDUS v3.0, CTEP suggested that any Late Adverse Event could be associated with the last treatment course that the patient received. With the v3.0 implementation, you now have a choice for those studies activated before 01/01/2002: you may continue to associate any Late Adverse Event with the last treatment course or you may submit the event in the Late Adverse Events record. For trials activated on or after 01/01/2002, see the *Late Adverse Event* section (section 2.2.3.9.3) of the *CDUS Instructions and Guidelines*.

22. If a patient's Off_Treatment_Reason is reported as "Withdrawal/Refusal prior to beginning protocol therapy," should the Last_Treatment_Date be supplied since they never actually began treatment?

The Last_Treatment_Date is not required if the following reasons are documented as the Off_Treatment_Reason:

- Patient withdrawal/refusal before beginning protocol therapy
- Disease Progression before active treatment
- No Treatment, per protocol criteria (see Note below)

  Note: 'No Treatment, per protocol criteria' was added as a valid value for the Off_Treatment_Reason data element during September of 2002. The code used for this value for FTP submissions is '13.'

a. I need clarification concerning the Last_TX_Date field and how it differs from the Treatment_Course_Start_Date for the patient's last cycle?

The Last_TX_Date is defined as the last day that the patient received treatment on their last treatment course. Treatment_Course_Start_Date is the date when a course of treatment begins. Each course of treatment will have its own Treatment_Course_Start_Date, but there is just one Last_TX_Date.

23. I see that one of the valid values for Off_Treatment_Reason is 'Disease Progression before Active Treatment.' How does CTEP define the term "active treatment?" Is it the point when the patient receives any chemo, the point when the patient receives any investigational drug, or the point before the patient receives any treatment on the study?

CTEP realizes that there might be limitations; however, "active treatment" would be considered any form of therapy identified in the schema of the protocol (e.g., surgery; radiation; commercial chemo agents; investigational agents). Please refer to the protocol schema for assistance. If further guidance is required, please send your query to the NCI CTEP Help Desk.

24. I do not always have all of the data required by the due date and it often changes after submitting. How do I proceed?

CTEP realizes that the data will constantly change and requests that you provide the most recent and accurate data known at the time of your submission.

In the event that the data within your submission will not be complete or will cause a rejection due to business rule associations, CTEP prefers you submit the incomplete data set as soon as possible followed by a complete data set by the end of the quarter or as soon as the data are available.

CTEP recommends that you select a Cut_Off_Date of at least one month in advance to provide for additional data collection and updating. For example, you may provide a Cut_Off_Date of June 30th for a July 31st submission due date. This would provide the month of July to obtain any missing data.

25. Does CTEP have a standard procedure on submitting Treatment Assignment Codes and Descriptions?

The *Treatment Assignment Instructions and Guidelines* have been posted to the CTEP Home page. The following information can be found in this document.

Treatment Assignment Instructions and Guidelines

1. Overview

A Treatment Assignment Code (TAC) and a Treatment Assignment Description (TAD) must accompany each clinical trial where a unique treatment characteristic is utilized to uniformly group patients for separate analysis of adverse events and response data.

The TAC is a unique identification code (e.g., 'Level 1') assigned to each treatment assignment and is limited to ten alphanumeric characters. Patients on trials utilizing a single treatment assignment are entered on a TAC such as 'TA1.'

The TAD is a complete description of each treatment assignment (e.g., Cisplatin 100mg/m^2 IV over 1 hour on Day 1, every 21 days and Taxol 130mg/m^2 IV over 3 hours on Day 1, every 21 days). The agent name, dose (including units), route, and frequency/schedule for every agent within the treatment assignment must be included. A brief description of any non-pharmacologic treatment modality(s) (e.g., radiation, surgery) is also required.

CTEP develops TACs and TADs for all studies utilizing a CTEP-held IND (investigational) agent. Each arm or dose level is considered a distinct treatment assignment. Occasionally, TACs are developed for components of a regimen (e.g., induction phase, consolidation phase, maintenance phase) versus an arm or dose level. The protocol document serves as the guide for developing TACs and TADs.

1.1 TAC Availability

TACs are available for **all** dose levels as noted below.

1.1.1 Dose De-Escalation

A dose reduction that results when a patient experiences a Dose Limiting Toxicity (DLT) in a dose escalation/de-escalation (typically Phase 1) trial. The protocol indicates which adverse events and their associated grade are considered to be a DLT. This applies most frequently to Phase 1 trials.

1.1.2 Dose Escalation

A dose increase that occurs if a patient meets the appropriate criteria, as stated in the protocol, and they are able to receive the higher dose level of drug (e.g., intra-patient dose escalation). This applies most frequently to Phase 1 trials.

1.1.3 Crossover

A defined point where a patient switches from one treatment arm to another treatment arm. This most frequently applies to randomized trials when disease progression occurs.

1.2 TAC Unavailability

TACs will not be available for the following dose adjustments.

1.2.1 Dose Modification

A dose reduction or a dose increase that results when a patient experiences an adverse event that has not been defined in the protocol as a DLT, or has a low-grade adverse event, or meets the criteria to increase a dose. Dose modifications most frequently apply to Phase 2 and 3 trials.

1.2.2 Individual Patient Titration

An incremental dose increase or decrease of a specified agent to eventually achieve a point of tolerance or blood level. This will be stated in the TAC description.

1.3 Examples

The following are examples of TAC specification throughout patient enrollment on a protocol.

1.3.1 TAC Change Required

A TAC is selected for each course the patient receives. The enrollment TAC is used for subsequent courses **unless** one of the following occurs:

- **Dose De-Escalation** – If a patient in a dose finding trial develops a DLT and, per protocol, the dose level is reduced, then a new TAC should be selected (i.e., course 1 TAC is 'Level 1,' DLT occurs, course 2 TAC would become 'Level -1' [minus one], to denote a decrease).

- **Dose Escalation –** If the protocol is a dose finding study and allows for intra-patient dose escalation, a new TAC should be selected (i.e., course 1 TAC is 'Level 1,' patient's dose increases, course 2 TAC would become 'Level 2').
- **Crossover –** If a patient with a planned crossover changes to the cross-over TAC (i.e., a patient is first randomized to either treatment 1 or treatment 2 and after disease progression on either treatment, is crossed over to either treatment 3 or treatment 4), then a new TAC should be selected. The crossover TACs will be clearly noted in the TAC description, even if the same dose is used.

1.3.2 TAC Change is NOT Required

A TAC is selected for each course the patient receives. The enrollment TAC will continue to be used even if the following criteria occur:

- **Dose Modification –** If a patient experiences an adverse event not considered to be a DLT based on the protocol, but does require a dose modification, or has a toxicity requiring dose reduction in a non-dose finding trial, then the patient's original TAC is used for data submission.
- **Individual Patient Titration –** If a patient has a dose changed because of their own outcome, whether planned or not (i.e., a patient who starts at a thalidomide dose of 200mg daily and is gradually increased to their own tolerance of 600mg), this will be stated in the TAC description and the original TAC is to be used for data submission.

26. The treatment on my protocol has patients crossing over from one treatment arm to another treatment arm. How do you suggest I number the courses for each of the arms (initial and cross over)?

CTEP recommends that courses be sequentially numbered using the Course ID data element. The Course ID can include up to six numbers to uniquely identify each course(s) on a trial. Be aware that CDUS does not support two Course IDs of the same number for the same patient. For a trial with crossover treatments, if a sequence of 1, 2, 3, etc., is used for the initial arm of treatment, then a sequence such as 11, 12, 13, etc., or 101, 102, 103, could be used for the crossover arm.

27. What is the procedure to address a Treatment Assignment, Subgroup, or Correlative Study code, description, or data discrepancy?

Requests to change a code identifier or the descriptions accompanying codes – All requests should be sent directly to the Protocol and Information Office (PIO) at pio@ctep.nci.nih.gov. If there are any concerns at this time, the PIO should be immediately contacted for a resolution prior to your first submission or before patients are accrued and assigned to a code (i.e., first CDUS submission or AdEERS report)

Requests for data clean-up within the CDUS database – The CDUS team should be alerted, via the NCI CTEP Help Desk, when there are data-related issues involving code updates and/or changes, as patients may need re-assignment.

Note: The Coordinating center is responsible for sending all codes and descriptions to participating sites at the time of protocol approval and when updates are sent from the PIO.

28. I have received a rejection of R0014 (Invalid Value) for a TAC that I thought was valid for my protocol. How should I proceed?

The lists of valid codes are provided to your organization when the protocol is approved by CTEP. As a reminder, the list of codes are distributed at the beginning of each quarter. Please review the most recent list to validate that the "invalid" TAC is not listed on this document. If this code is present, please validate that the code is exactly the same as the code you are submitting. If the invalid code is not listed, then e-mail the Protocol and Information Office at pio@ctep.nci.nih.gov to query why the TAC is not on the list of codes.

All CDUS valid TACs must not only be abstracted to the CTEP database based on the criteria outlined in the protocol, but must also be quality checked before they are considered valid.

Please refer to the *Treatment Assignment (arm/dose level)* section (section 2.1.2.3) of the *CDUS Instructions and Guidelines* for more information.

29. There are Correlative Studies embedded in my protocol. Some of my data should not be submitted until the data can be batched and analyzed. How do I submit in the meantime?

Presently (as of CDUS, v3.0), there are four fields for reporting Correlative Study data: Patients_Collected, Patients_Analyzed, Samples_Collected, and Samples_Analyzed. If a Correlative Study is embedded in your protocol and activated on or after 01/01/2002, you are required to submit data to all four fields with each CDUS submission. If it is too early to submit fully analyzed data, then enter the value '0' (zero) and provide an explanation under Trial_Comments to provide clarification.

30. I have a patient who has several documented (partial, complete, and progression) responses. What do I submit to CTEP via the CDUS?

You must submit all confirmed (confirmed as per protocol defined criteria) responses via CDUS. Responses *must* follow a logical flow (e.g., a Complete Response may follow a Partial Response; however, a Partial Response may not follow a Complete Response). The correct logical flow for the responses identified above would be Partial Response followed by Complete Response, followed by Progression.

31. Should 'Progression' be submitted if that is the only confirmed response my patient has had?

Yes. If 'Progression' is the only confirmed response for your patient, then the response of 'Progression' would be the only response submitted. If there were confirmed responses before the response of 'Progression,' then all confirmed responses, including 'Progression,' are reported.

32. How do I determine the Observed Date for my response? Is this documented in my protocol?

An Observed Date is mandatory for all submitted responses. The Observed Date is defined as the date for each category of response that the patient's disease was shown to have objectively responded to therapy (e.g., date of radiographic scan) sufficient to meet the protocol-specified criteria for that category of response.